

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 7/16</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 95/33441</b> <b>(43) International Publication Date:</b> 14 December 1995 (14.12.95)
<b>(21) International Application Number:</b> PCT/US95/07149 <b>(22) International Filing Date:</b> 5 June 1995 (05.06.95)  <b>(30) Priority Data:</b> 08/254,178                      6 June 1994 (06.06.94)                      US  <b>(71) Applicant:</b> BLOCK DRUG COMPANY, INC. [US/US]; 257 Cornelison Avenue, Jersey City, NJ 07302 (US).  <b>(72) Inventors:</b> GINGOLD, James, L.; 55 North Star Drive, Morristown, NJ 07960 (US). MARKOWITZ, Kenneth, J.; 54 Glenwood Road, Fanwood, NJ 07023 (US). YEH, Kuo- Chen; 210 Gold Edge, Westfield, NJ 07090 (US). BUELO, Adonis; 76 Boyd Avenue, Jersey City, NJ 07304 (US). HERMS, James, K.; 282 Eighth Street, Jersey City, NJ 07302 (US). SYNODIS, Joseph; 66 Rotary Drive, Summit, NJ 07901 (US).  <b>(74) Agents:</b> MEILMAN, Edward, A. et al.; Ostrolenk, Faber, Gerb & Soffen, 1180 Avenue of the Americas, New York, NY 10036 (US).		<b>(81) Designated States:</b> AU, BR, CA, FI, JP, KR, MX, NZ, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> RELIEF OF DENTINAL HYPERSENSITIVITY BY SUBMICRON PARTICLES  <b>(57) Abstract</b>  Phosphate-free oral compositions containing cationically charged colloids are effective to treat tooth hypersensitivity.		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

- 1 -

RELIEF OF DENTINAL HYPERSENSITIVITY  
BY SUBMICRON PARTICLES

BACKGROUND OF THE INVENTION

1. Field of the Invention

5           This invention relates to compositions and methods for treating hypersensitive teeth using materials having reduced abrasive properties.

2. Description of Related Art

10           Dental hypersensitivity is a frequently encountered problem in dentistry and a very troublesome clinical complaint. Hypersensitivity can cause pain and discomfort as a result of a variety of conditions such as changes in temperature, pressure, chemical or osmotic action. Exposure of the dentin frequently leads to  
15           hypersensitivity. Dentin exposure may occur due to abrasion, recession of the gums, attrition, periodontal disease, improper dental care and the like. The usual methods of treating hypersensitive teeth often employ a desensitizing dentifrice or solution.

20           One approach to desensitizing teeth is to occlude exposed dental tubules. These fluid filled tubules lead from the pulp to the surface of the dentin. When the surface of the tooth is eroded, the dental tubules become exposed to the external environment. The  
25           exposed dentinal tubules provide a pathway for the transmission of external stimuli, such as changes in temperature, pressure, ionic gradients and the like, directly to the pulpal nerves causing a strong pain

- 2 -

response by the nerve. Blocking the tubules reduces the effects of the external stimuli on the nerve, thereby reducing or eliminating any pain response by the nerve.

5       Tubule occluding agents may be administered in a variety of ways. Dentifrice compositions, including pastes and gels, may be used, mouthwashes or oral rinses may be used, and professionally applied coatings may also be used to deliver tubule occluding agents to the dentin.

10       Many agents assumed to be effective in the treatment of sensitive teeth are known. Some of these treatments have been demonstrated to be capable of occluding the dentinal tubules. For example, U.S. Patent No. 3,122,483 to Rosenthal, issued February 25, 1964, teaches the use of strontium ions as a desensitizing  
15       agent. Related patents include U.S. Patent No. 3,699,221 to Schole et al., issued October 17, 1992; U.S. Patent No. 4,990,327 to Neirinckx, issued February 5, 1991; and U.S. Patent No. 5,087,444 to Jackson et al., issued February 11, 1992. U.S. Patent No. 4,224,310 to Shah,  
20       issued September 23, 1992, is directed to Strontium EDTA, while a water soluble strontium and potassium salt in combination is the mentioned by European Application No. 390,456. U.S. Patent No. 5,015,465 to Straw, issued May 14, 1991, is directed to strontium salts such as  
25       acetates, chlorides, nitrates, lactates and bromides. U.S. Patent No. 4,057,621 to Pashley et al., issued November 8, 1977, and U.S. Patent No. 4,538,990 also to Pashley, issued September 3, 1985, are directed to the use of an alkaline metal or ammonium oxylate. U.S.  
30       Patent No. 3,863,006 to Hodosh, issued January 28, 1975, is directed to the use of an alkali metal nitrate. Citric acid and sodium citrate are mentioned in U.S. Patent No. 4,011,309 to Lutz, issued March 8, 1977, while

- 3 -

calcium chloride dihydrate, magnesium chloride hexahydrate, sodium chloride and potassium bicarbonate are mentioned in U.S. Patent No. 3,689,636 to Svajda, issued September 5, 1972. Potassium and strontium  
5 nitrate are mentioned in U.S. Patent No. 4,933,171 to Bristow et al., issued June 12, 1990, while the use of copolymers to form a protective barrier covering the dental tubules is mentioned in U.S. Patent No. 5,133,957 to Suh et al., issued July 28, 1992. British Patent No.  
10 2,239,601 teaches the combination of an alkaline metal salt with a chloride, nitrate, sulphate or acetate of a group II metal or aluminum or a polymerizable monomer to form a protective coating over the tubules.

The use of particulate materials as  
15 desensitizers is also generally known. Thus U.S. Patent 4,992,258 to Mason, issued February 12, 1991, is directed to the use of montmorrolinite clay having a particle size of less than 2 microns as being effective for blocking dental tubules using dentin hydraulic conductance  
20 chamber. In U.S. Patent No. 4,645,622 to Nakashima et al., issued February 24, 1987, the dental tubules, which are indicated to have a diameter in the range of about 1-3 microns, are occluded or constricted by employing soluble aluminum carboxylate compounds. The other  
25 components of the composition are selected so as not to reduce the number of available aluminum ions. Alumina in a concentration of 5-50% is suggested as an abrasive. U.S. Patent No. 4,634,589 to Scheller, issued January 6, 1987, is directed to the use of apatite having an average  
30 particle size of less than 8 microns, preferably less than 4 microns, as a desensitizer to occlude dentinal tubules. Apatite is composed of calcium phosphate, calcium phosphate fluoride, and calcium carbonate

- 4 -

phosphate. The use of amorphous calcium compounds applied to dentinal tissue to rapidly form apatite in situ, thus remineralizing the teeth and purportedly reducing dentinal hypersensitivity, is taught in U.S. Patent No. 5,037,639 to Tung, issued August 6, 1991.

The use of small particle sized materials in dental compositions for a variety of purposes, other than desensitization, is known. As an example, U.S. Patent No. 4,612,191 to Yeh et al., issued September 16, 1986, is directed to the use of a combination of anhydrous aluminum silicate (available commercially as Kaolin or Kaopolite) having a particle size of less than 1 micron and silica particles for a stain removal abrasive system. U.K. Patent No. 1,449,317 shows 0.1-50 micron polymer particles in a low abrasive dentifrice. Similarly, U.S. Patent No. 4,986,981 to Grace et al., issued January 22, 1981, discloses a low abrasion toothpaste for removing plaque, mucin and tartar, whose abrasive system includes 1 micron alumina. Use of 1-15 micron hydroxyapatite as an abrasive in an oral desensitizer composition is discussed in U.S. Patent No. 4,933,171 to Bristow et al., issued June 12, 1990.

U.S. Patent No. 5,244,651 to Kavane, issued September 14, 1993, is directed to a method of desensitizing hypersensitive dentin. The method comprises treating teeth with a combination of a salt of a polyvalent metal and a polyol phosphate. This combination produces a colloid of metal hydroxides. Apparently, the colloid is stabilized by the phosphate compound. The compound is prepared by combining the chloride, sulfate, or nitrate salt of magnesium, strontium, barium, zinc, iron titanium, aluminum, chromium, manganese, copper, nickel, cobalt, bismuth,

tin, vanadium, molybdenum, niobium, zirconium, antimony, indium, or a lanthanoid with a polyol phosphate in acidic or neutral aqueous medium. The medium is then adjusted to neutral pH. Preferred phosphates include glycerol phosphate.

5 Despite the time honored use of alumina particles in dental compositions as abrasives, desensitization properties have not been directly attributed to this material. (See Mostafa, et al., J. Dent. Res. 1983; 62 (Spec. Issue): 433 (Abstr. 165).  
10 Mostafa et al. have shown that abrasive materials (alumina, silica calcium carbonate etc.) interact with dentin as seen in SEM photomicrographs and concluded that abrasives may have an important role in reducing dentin  
15 hypersensitivity by blockage of tubules. But, applicants have discovered that abrasive and polishing grade alumina, aluminum oxide and aluminum silicate are ineffective for reducing dentinal fluid flow through dentin disks. It was therefore surprising and unexpected  
20 to discover that cationically charged colloidal particles, including alumina, were effective in reducing dentinal flow by occluding the dentinal tubules.

Some agents are known to form mineral deposits on the surfaces of the exposed dental tubules while in  
25 some cases, the abrasive action from brushing may cause a smear layer to form over the surface of the tooth and thus plug up the open tubules. The accumulation of particulate matter from the interstitial fluid passing through the dental tubules or remineralization within the  
30 tubules can also cause a natural occlusion of the tubules.

One difficulty presented by using occlusive dentifrice treatments for hypersensitive teeth is that

the act of brushing the teeth, particularly with an abrasive dentifrice, can dislodge occlusive materials from the tubules, especially newly added materials residing at the entrance to the tubules.

5     SUMMARY OF THE INVENTION

The principal object of the present invention therefore is to provide a new dentinal desensitizing agent and compositions containing that agent.

10     An additional object of the invention is to provide a composition having reduced abrasion levels to thereby reduce the deleterious effect of highly abrasive compositions on tubule occlusion.

15     Still another object of the invention is to provide a method for treating hypersensitive teeth with the desensitizing agent of the invention.

One advantage of the invention is that the desensitizing agent of the invention may also act as an abrasion reducing agent.

20     Additional objects and advantages of the invention will be set forth in part in the description that follows, and in part will be obvious from this description, or may be learned by practice of the invention. The objects and advantages of the invention may be realized and attained by means of the  
25     instrumentalities and combinations particularly pointed out in the appended claims.

30     To achieve the foregoing objects and in accordance with the purpose of the invention, as embodied and broadly described herein, the invention provides a composition containing cationically charged colloidal particles for treating hypersensitive teeth.



- 7 -

To further achieve the foregoing objects and in accordance with the purpose of the invention, the invention further provides a method for treating a hypersensitive tooth by applying a composition containing cationically charged colloidal particles to at least the affected region of the tooth.

Other features and advantages of the present invention will become apparent from the following description of the invention which refers to the accompanying drawings.

#### DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

Reference will now be made in detail to the presently preferred embodiments of the invention.

In accordance with the present invention, cationically charged colloidal particles are used as a dental desensitizing agent. The particles may be employed in conjunction with a dentally acceptable carrier and can be formulated into any type of oral composition such as an aqueous suspension, dentifrice, gel, mouthwash, lozenge, buccal adhesive patch, gum or other oral composition whose use on a periodic basis can provide relief from the pain and discomfort of hypersensitive teeth.

Preferably the particles of the invention are selected from compounds comprising metals from groups IB, IIA, IIB, IIIA, IIIB, IVB, VA, VB, VIA, VIB, VIIB, and VIIIB of the Periodic Table, including the Lanthanides. For economic reasons, it is preferred that the metals are selected from commonly occurring compounds, such as alumina, and the compounds should be non toxic. Preferably the metals are selected from the group consisting of: Y, Ti, V, Cr, Mn, Fe, Co, Cu, Zn, Al, Mg,

- 8 -

Ca, Sr, Ba, Zr, Ag, Sn, Bi, W, Ce, La, Pr, Nd, and Sc. More preferably, the metals are selected from the group consisting of: Y, Ce, Al, and Zr. Most preferably, the metal is aluminum or zirconium.

5           The compounds must be capable of forming colloids in aqueous environments, either alone or in conjunction with suitable buffers. The colloids formed from these compounds must also be capable of holding a cationic charge in the aqueous environments ordinarily  
10 found in the oral cavity. Preferably, the compounds are relatively less expensive, stable, non-toxic compounds, like some halides, silicates, acetates, oxides and hydroxides. Most preferably, the compounds are oxides.

          Cationically charged colloidal alumina has  
15 heretofore been used for a variety of applications such as, for instance, a binder in glass and ceramic systems, a catalyst support, a reinforcing agent, a dust or dirt repellent and in waterproofing compositions. This type of alumina is commercially available and the submicron  
20 particles have usually been surface treated so as to impart a positive surface charge thereon. Any of these commercially available materials can be employed in the process and products of the present invention as long as the colloid is dentally acceptable. One example of a  
25 commercially available product is that sold under the trademark Nalco 8676 and this alumina has an average particle size of about 2 nm (0.002  $\mu\text{m}$ ). The alumina can also be in the form of a coating on another material such as silica, in which case the submicron size is of the  
30 entire particle and not just the alumina. An example is sold under the trademark Nalco 1056 and is alumina-coated silica particles whose average size is 20 nm (0.02  $\mu\text{m}$ ). The two named commercially available products are in the

- 9 -

form of an aqueous colloidal dispersion of the submicron alumina particles. Such aqueous dispersions can often be used as such in order to formulate the dental compositions of the present invention and it is not  
5 necessary to separate the particles of alumina from the dispersion.

In general, the particle size is submicron and is usually up to about 0.1  $\mu\text{m}$ . The colloid particles often are in the range from about 0.001 to about 0.2  $\mu\text{m}$   
10 and preferably from about 0.001 to about 0.025  $\mu\text{m}$ .

The compound is incorporated into the dental composition in a desensitizing effective amount. This will vary depending on the particular type of oral composition and other materials present but most often,  
15 the agent will be an amount of about 0.1 to 10%, usually about 1 to 5% and most preferably about 3 to about 5%. Larger amounts of the compound can also be employed if so desired.

The compound can be incorporated into any type  
20 of oral dental composition as long as the cationic surface charge of the desensitizing agent is not completely neutralized. It is preferred that the amount of neutralization of that charge be minimal. By combining the compound with a suitable dentally  
25 acceptable carrier, the dental oral composition can take the form of a dentifrice, mouthwash, lozenge, buccal adhesive patch, gel or gum and the like. The other ingredients used to formulate such compositions and the procedures employed are well known and commonly used in  
30 preparing these oral compositions. Thus, for instance, it is possible to incorporate a fluoride source into the oral composition and it is also possible to formulate the oral compositions in conjunction with additional

- 10 -

desensitizing agents. Such additional desensitizing agents include, without limitation, strontium chloride and other strontium containing compounds, potassium nitrate, sodium silicofluoride, zinc chloride, potassium chloride, potassium bicarbonate and glycerine. In toothpaste formulations, the submicron compound of the invention generally does not provide sufficient abrasive/polishing activity and therefore the use of known abrasives such as larger particle sized alumina or silica will normally be incorporated in the composition.

But, one surprising advantage of cationically charged colloidal alumina is that its presence can materially reduce the abrasion levels of dentifrices. This reduced abrasion helps to offset loss of some of the occluding material that would otherwise be lost through abrasive scouring action during brushing. Thus, added abrasives will not have as direct an effect on abrasion of the dentin as in ordinary dentifrices.

In order to further illustrate the present invention, various non-limiting examples are set forth below. In these examples, as throughout the specification and claims, all temperatures are in degrees centigrade and all parts and percentages are by weight unless otherwise indicated.

#### 25     EXAMPLES 1-4

In order to test the desensitizing properties of potential desensitizing agents, four different aluminum containing particles were mixed with water and the resulting oral compositions tested using the method described in Pashley, "Dentin permeability: Theory and practice", Experimental Endodontics, Spangberg, ed. CRC Press 1989). This test measures the flow of fluid through

- 11 -

a sliced dentin disk. A treatment that will reduce the flow through the disk can also result in reduced dentinal hypersensitivity for people using the treatment.

5 A caries-free tooth is sliced to obtain a 0.4 to 0.6 mm thick dentin disk. The disk is mounted on a split chamber device as described in the Journal of Dental Research, 57:187, 1978. The initial flow of fluid through the disk is measured and then the disk is exposed to human saliva and treated by brushing with one of the  
10 desensitizing treatments. After brushing, the flow rate is again measured and the reduction in flow is calculated from these measurements. The results are set out in Table 1.

15	Table 1			
	Particulate	Particle Size	Concentration Percent	Flow Reduction
	Aluminum silicate	1.0 $\mu\text{m}$	5%	9.5
	Aluminum hydroxide	0.5 $\mu\text{m}$	10%	24.1%
	Uncharged alumina	0.013 $\mu\text{m}$	17%	19.3%
	Cationic alumina	0.002 $\mu\text{m}$	5%	93.4%

20 These results confirm that the presence of a cationic charge on submicron alumina drastically reduces tubular flow even though the concentration of the particulate had been reduced by a factor greater than three.

25 EXAMPLES 5-13

Example 4 was repeated varying the concentration of the alumina and adjusting the pH with sodium hydroxide. The results are set out in Table 2.

- 12 -

5

10

Table 2		
pH	Concentration %	Flow Reduction %
5	0.13	46.3
5	1.0	86.4
5	2.4	88.2
5	8	89.8
5.5	0.98	84.1
6	.22	38.6
6	0.48	51.8
6	0.95	65.8

EXAMPLES 14-18

Example 5 was repeated with 0.02 micron alumina-coated silica particles. The results are set out in Table 3.

15

20

Table 3		
pH	Concentration %	Flow Reduction %
8	15	37.4
4.5	15	90.5
4	15	96.2
5	22.0	28.5
3.5	30.0	100

A desensitizing solution is made from the following ingredients:

INGREDIENT	WEIGHT % (approx.)
Colloidal Dispersion of alumina (10%)	30 %
Sodium Chloride	0.6%
Water	69.4%

25

- 13 -

EXAMPLE 20

A desensitizing mouth wash is made from the following ingredients:

	<u>INGREDIENT</u>	<u>WEIGHT % (approx.)</u>
5	Colloidal Dispersion of alumina (10%)	25 %
	Potassium Nitrate	5 %
	Nonionic Surfactant (Pluronic F-127)	5 %
	Ethanol	10 %
	Glycerin	10 %
10	Sodium Saccharin, Flavor	0.1%
	Preservative, Dyes	

EXAMPLE 21

A desensitizing chewing gum is prepared from the following ingredients:

	<u>INGREDIENT</u>	<u>WEIGHT % (approx.)</u>
15	5 Chewing Gum Base	24.64%
	Glycerin	1 %
	Calcium Saccharin	0.06%
	Sorbitol (Powder)	53.5 %
20	Lyzasin	13 %
	10 Lecithin	0.8 %
	Flavor	1 %
	Colloidal Dispersion of Alumina (10%)	6 %

EXAMPLE 22

25 A desensitizing lozenge is prepared from the following ingredients:

	<u>INGREDIENT</u>	<u>WEIGHT % (approx.)</u>
	Sorbitol	86.5%
	Xylitol	6 %
30	Citric Acid	0.4%
	Colloidal Dispersion of Alumina (10%)	7 %
	Flavor	0.1%

EXAMPLE 23

- 14 -

A desensitizing topical gel is prepared from the following ingredients:

	<u>INGREDIENT</u>	<u>WEIGHT % (approx.)</u>
	Water	33.4%
5	Glycerin	6 %
	Sorbitol	6 %
	Colloidal Dispersion of Alumina (10%)	24 %
	Potassium Nitrate	5.0%
	Pluronic F-127	25
10	Flavor, Preservative and Dye	0.6%

EXAMPLE 24

A desensitizing dentifrice is prepared from the following ingredients:

	<u>INGREDIENT</u>	<u>WEIGHT % (approx.)</u>
15	Water	38 %
	Potassium Nitrate	5.0%
	Sylodent 750 (hydrated silica)	0.2%
	Sodium Fluoride	0.2%
	Carboxymethyl Cellulose	2.0%
20	Glycerin	20 %
	GAQUAT 755N (20%)	4.0%
	Colloidal Dispersion of Alumina (10%)	30 %
	Flavor and Preservatives	0.6%

EXAMPLE 25

25 In order to demonstrate that the colloidal alumina particles reduce abrasion, six laboratory batch dentifrices were prepared using various desensitizing dentifrice formulations. 10% by weight Tixocile abrasive, a silica abrasive manufactured by

30 Rhone-Poulenc, was added to each batch to increase the amount of abrasives in the dentifrice and thereby to accentuate the effect of the colloidal alumina on the system. 10% by weight Nalco beads were added to three of the batches and all six batches were measured, using the

35 standard test, for "Radioactive Dentin Abrasion" (RDA).



- 15 -

This value is reported in Tables 4 and 5 as "A.I.," the "abrasion index." The results are reported with their associated Standard Error of Mean values.

Table 4		
5	FORMULA DESCRIPTION	A.I. Index ( $\pm$ SEM) RANGE
	Sensodyne SC type 10%Tixosil 73 10% Nalco	$31 \pm 1$ 29-33
10	Sensodyne SC type 10% Tixosil 73	$37 \pm 4$ 24-52
	KNO <sub>3</sub> /MFP T.P. 10% Tixosil 73, 10% Nalco	$57 \pm 2$ 42-56
15	KNO <sub>3</sub> /MFP T.P. 10% Tixosil 73	$69 \pm 3$ 57-78
	KNO <sub>3</sub> /NaF T.P. 10% Tixosil 73 10% Nalco	$23 \pm 1$ 18-30
20	KNO <sub>3</sub> /NaF T.P. 10% Tixosil 73	$62 \pm 2$ 54-69

For clarity, the data set out in Table 4 is summarized in Table 5 and compared against tests run on Crests brand Regular Flavor toothpaste.

Table 5		
25	FORMULA DESCRIPTION	A.I. $\pm$ SEM
		WITHOUT NALCO WITH NALCO
	KNO <sub>3</sub> /MFP/TIXOSIL 73	$69 \pm 3$ $51 \pm 2$
	KNO <sub>3</sub> /NaF/TIXOSIL 73	$62 \pm 2$ $23 \pm 1$
	SrCl <sub>2</sub> .6H <sub>2</sub> O/TIXOSIL 73	$37 \pm 4$ $31 \pm 1$
	CREST	$115 \pm 1$ --

EXAMPLE 26

Dentin flow reduction examples similar to those carried out on colloidal alumina as set forth in Example 1, were carried out on 5-10 nm particle size zirconia, ZrO<sub>2</sub>, obtained from P.Q. Corporation, and sold under the trade name NYACOL. The results are set out in Table 6.

<u>Table 6</u>	
<u>Solution Strength</u>	<u>Dentin Flow Reduction</u>
20.0%	98.5%
2.0%	91.4%
0.5%	83.8%
0.25%	77.2%
0.1%	14.0%

EXAMPLE 27

An dentifrice was prepared to demonstrate the utility of one embodiment of the invention. The dentifrice composition set out below provided a flow reduction of 74.2%.

<u>Dentifrice</u>	<u>Water Percent (approx.)</u>
<u>Ingredient</u>	
Water	30.9 %
Potassium chloride	3.75 %
Colloidal zirconia	10.0 %
acetate solution, (35%)	
Glycine	10.0 %
Sorbitol solution (70%)	12.0 %
Fumed silica	1.0 %
Hydrated silica	12.0 %
Glycerin	12.0 %
Hydroxyethyl cellulose	1.6 %
Cocamidopropyl betaine	5.0 %
Flavor	1.5 %
Sodium fluoride	0.243%

- 17 -

EXAMPLE 28

A buffered paste was prepared and tested in accordance with the procedure set forth in Example 1. The paste showed a flow reduction of 95%. The formulation of the buffered paste is set forth below.

Buffered Paste	
<u>Ingredient</u>	<u>Weight Percent</u>
Colloidal zirconia acetate solution, (35%)	10 %
Glycine	10 %
Sorbitol solution (70%)	4.3%
Amphoteric surfactant	3 %
Kaopolite	15 %
Hydrated silica abrasive	20 %
Water	37.5%

EXAMPLE 29

NYACOL Colloidal yttria, also obtained from P.Q. Corporation, was tested in accordance with the procedure set forth in Example 1 to determine its tubule blocking abilities. A colloidal solution was prepared containing the following ingredients:

<u>Ingredient</u>	<u>Weight Percent</u>
Yttria (yttrium oxide $Y_2O_3$ )	4.2%
Potassium nitrate	5.0%
Water	90 %

The Yttria had a particle size of about 5 nm and displayed a flow reduction of 75.2%.

EXAMPLE 30

NYACOL Colloidal ceria also obtained from P.Q. Corporation was tested in accordance with the procedure set forth in Example 1 to determine its tubule blocking

- 18 -

abilities. A buffered colloidal solution was prepared containing the following ingredients:

<u>Ingredient</u>	<u>Weight Percent</u>
Ceria (cerium oxide $\text{CeO}_2$ )	4.0 %
5 Glycine	10.0 %
Potassium nitrate	5.0 %
Water	80.75%

The ceria had a particle size of about 15 nm and displayed a flow reduction of 75.6%.

10 The purpose of the above description is to illustrate some embodiments of the present invention without implying a limitation. It will apparent to those skilled in the art that various modifications and variations may be made in the apparatus or procedure of the invention without departing from the scope or spirit of the invention.

15 Although the present invention has been described in relation to particular embodiments thereof, many other variations and modifications and other uses will become apparent to those skilled in the art. It is preferred, therefore, that the present invention be 20 limited not by the specific disclosure herein, but only by the appended claims.

WHAT IS CLAIMED IS:

1. A phosphate-free composition for treating hypersensitive teeth comprising a cationically charged colloid.

2. The composition of claim 1, wherein said colloid comprises a metal compound selected from the group consisting of: metals of groups IB, IIA, IIB, IIIA, IIIB, IVA, IVB, VA, VB, VIB, VIIB, and VIIIB of the Periodic Table, and the Lanthanides.

3. The composition of claim 2, wherein said colloid comprises a metal compound selected from the group consisting of: Y, Ce, Al, and Zr compounds.

4. The composition of claim 2, wherein said colloid comprises a metal halide, oxide, hydroxide, silicate or acetate.

5. The composition of claim 1, wherein said composition further comprises a suitable carrier for said cationically charged colloid selected from the group consisting of: aqueous suspensions, dentifrices, gels, mouthwashes, lozenges, buccal adhesive patches, and chewing gums.

6. The composition of claim 5, further comprising a second desensitizing agent.  
no

7. The composition of claim 1, wherein the particle size of said cationically charged colloid is from about 0.001  $\mu\text{m}$  to about 0.2  $\mu\text{m}$ .

-20-

8. The composition of claim 7, wherein said cationically charged colloid comprises up to about 10% by weight of said composition.

9. The method for treating a hypersensitive tooth comprising the step of applying to the surface of said tooth a phosphate-free composition comprising an amount of cationically charged colloid sufficient to at least partially desensitize said tooth.

10. The method of claim 9, wherein said composition further comprises a suitable carrier for said cationically charged colloid selected from the group consisting of: aqueous suspensions, dentifrices, gels, mouthwashes, lozenges, buccal adhesive patches, and chewing gums.

11. The method of claim 9, further comprising a second desensitizing agent.

12. The method of claim 9, wherein the particle size of said cationically charged colloid is from about 0.001  $\mu\text{m}$  to about 0.2  $\mu\text{m}$ .

13. The method for manufacturing a treatment for hypersensitive teeth comprising the step of suspending an effective amount of cationically charged colloid in a suitable phosphate-free carrier to form a desensitizing composition.

-21-

14. The method of claim 13, further comprising the step of incorporating a second desensitizing agent into said composition.

15. The method of claim 13, wherein the particle size of said cationically charged colloid is from about 0.001  $\mu\text{m}$  to about 0.2  $\mu\text{m}$ .

16. A method for achieving an effect in a patient comprising administering an effective amount of a phosphate-free composition comprising a cationically charged colloid to at least one hypersensitive tooth of said patient, wherein the effect is at least partial desensitizing of said tooth.

17. The method of claim 16, wherein the particle size of said cationically charged colloid is from about 0.001 $\mu\text{m}$  to about 0.2  $\mu\text{m}$ .

18. The use of a phosphate-free cationically charged colloid as an abrasion reduction agent.

19. A dentifrice comprising a phosphate-free cationically charged colloid, wherein said colloid comprises a compound selected from the group consisting of: alumina, zirconia, ceria and yttria.

20. A phosphate-free oral rinse, mouthwash or desensitizing sealant comprising a cationically charged colloid, wherein said colloid comprises a compound selected from the group consisting of: alumina, zirconia, ceria and yttria.

## INTERNATIONAL SEARCH REPORT

 International application No.  
PCT/US95/07149

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A 61K 7/16

US CL : 424/49

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/49

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 3,718,584 (BESTE et al.) 27 February 1973. See entire document.	1 to 5, 7, 8, 13, 15, 18
X	US, A, 4,545,923 (GRADEFF et al.) 08 October 1985. See entire document.	1 to 5, 7, 8, 13, 15, 18
X	US, A, 4,647,401 (GRADEFF et al.) 03 March 1987. See entire document.	1 to 5, 7, 8, 13, 15, 18
X	US, A, 4,714,567 (ROHN) 22 December 1987. See entire document.	1 to 5, 7, 8, 13, 15, 18



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

19 SEPTEMBER 1995

Date of mailing of the international search report

29 SEP 1995

 Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

SHEP ROSE

aco

Telephone No. (703) 308-1235



## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US95/07149

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4,913,840 (EVANS et al.) 03 April 1990. See entire document.	1 to 5, 7, 8, 13, 15, 18
X	US, A, 5,030,097 (TOBEY) 09 July 1991. See entire document.	1 to 5, 7, 8, 13, 15, 18
A	US, A, 5,224,651 (KAYANE et al.) 14 September 1993.	1 to 20
Y, P	US, A, 5,330,749 (GIACIN et al.) 19 July 1994. See entire document.	1 to 20
Y	US, A, 5,302,373 (GIACIN et al.) 12 April 1994. See entire document.	1 to 20
Y	US, A, 5,130,146 (TSUJITA et al.) 14 July 1992. See entire document.	1 to 20
Y	US, A, 5,049,375 (TSUJITA et al.) 17 September 1991. See entire document.	1 to 20
Y	US, A, 3,998,973 (CARLSON) 21 October 1976	1 to 20